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[Intervention Review]

Compression for preventing recurrence of venous ulcers

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ABSTRACT

Background

Up to 1% of adults will have a leg ulcer at some time. The majority of leg ulcers are venous in origin and are caused by high pressure in the veins due to blockage or weakness of the valves in the veins of the leg. Prevention and treatment of venous ulcers is aimed at reducing the pressure either by removing/repairing the veins, or by applying compression bandages/stockings to reduce the pressure in the veins.

The majority of venous ulcers heal with compression bandages, however ulcers frequently recur. Clinical guidelines therefore recommend that people continue to wear compression, usually in the form of hosiery (tights, stockings, socks) after their ulcer heals, to prevent recurrence.

Objectives

To assess the effects of compression (socks, stockings, tights, bandages) in preventing the recurrence of venous ulcers. If compression does prevent ulceration compared with no compression, then to identify whether there is evidence to recommend particular levels of compression (high, medium or low, for example), types of compression, or brands of compression to prevent ulcer recurrence after healing.

Search methods

For this second update we searched The Cochrane Wounds Group Specialised Register (searched 4 September 2014) which includes the results of regular searches of MEDLINE, EMBASE and CINAHL; The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2014, Issue 8).

Selection criteria

Randomised controlled trials (RCTs) evaluating compression bandages or hosiery for preventing the recurrence of venous ulcers.

Data collection and analysis

Two review authors undertook data extraction and risk of bias assessment independently.

Main results

Four trials (979 participants) were eligible for inclusion in this review. One trial in patients with recently healed venous ulcers (n = 153) compared recurrence rates with and without compression and found that compression significantly reduced ulcer recurrence at six months (Risk ratio (RR) 0.46, 95% CI 0.27 to 0.76).

Two trials compared high-compression hosiery (equivalent to UK class 3) with moderate-compression hosiery (equivalent to UK class 2). The first study (n=300) found no significant reduction in recurrence at five years follow up with high-compression hosiery compared with moderate-compression (RR 0.82, 95% CI 0.61 to 1.12). The second study (n = 338) assessed ulcer recurrence at three years follow up and found that high-compression hosiery reduced recurrence compared with moderate-compression (RR 0.57, 95% CI 0.39 to 0.81).

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Statistically significant heterogeneity precluded meta-analysis of the results from these studies. Patient-reported compliance rates were reported in both trials; there was significantly higher compliance with medium-compression than with high-compression hosiery in one and no significant difference in the second.

A fourth trial (166 patients) found no statistically significant difference in recurrence between two types of medium (UK class 2) compression hosiery (Medi versus Scholl: RR 0.74, 95% CI 0.45 to 1.2).

No trials of compression bandages for preventing ulcer recurrence were identified.

Authors' conclusions

There is evidence from one trial that compression hosiery reduces rates of reulceration of venous ulcers compared with no compression. Results from one trial suggest that recurrence is lower in high-compression hosiery than in medium-compression hosiery at three years whilst another trial found no difference at 5 years. Rates of patient intolerance of compression hosiery were high. There is insufficient evidence to aid selection of different types, brands, or lengths of compression hosiery.

PLAIN LANGUAGE SUMMARY

Compression hosiery (stockings) for preventing venous leg ulcers returning

Venous leg ulcers (open wounds on the lower leg) can be caused by a blockage or breakdown in the veins of the legs. Compression, using bandages or hosiery (stockings), can help heal most of these ulcers and is also widely used after healing to prevent ulcers returning. One small trial confirms that compression reduces ulcer recurrence compared with no compression. There is some evidence that people wearing high rather than moderate-compression hosiery are less likely to get a new ulcer. It is not clear whether moderate strength hosiery is better tolerated than high compression. There is, therefore, some evidence that compression hosiery might prevent ulcers, but the evidence is not strong.

BACKGROUND

Description of the condition

Venous ulceration is a chronic recurring condition. Callam found that 45% of people with ulcers in a study in Scotland had open leg ulcers for more than 10 years (Callam 1985). There is a considerable cost to the patient in terms of prescription charges (dressings, drugs and bandages), increased laundry bills due to discharge from the ulcer, time off work attending nurse/doctor consultations, and pain, isolation and distress (Charles 1995). The treatment of leg ulceration is extremely costly to the health service (the UK NHS was estimated to have spent £300 million in 1992), mainly in terms of nursing time (Bosanquet 1992).

Around 1% of adults in industrialised countries are affected by leg ulceration at some time in their life (Baker 1991). Around three-quarters of leg ulcers are caused by changes in the blood flow in the veins of the legs. These changes are caused by blockage (occlusion) and/or weakness in the valves of the veins (venous incompetence) (Callam 1985). The resulting ulcers are known as venous, stasis or varicose ulcers.

Occlusion and/or incompetence of the veins in the legs leads to increased pressure in the veins. This can sometimes be seen as distended, tortuous (varicose) veins. Increased pressure in the veins may cause varicose eczema, oedema in the lower leg, and deposition of scar tissue (fibrin) and iron pigments in the skin. This may lead to breakdown of the skin, or can delay healing if the leg is injured.

Both treatment of venous ulcers and prevention of recurrence aims to reduce the pressure in the veins. This can be accomplished by surgical removal of superficial or perforating veins (or both) or blocking any incompetent veins by injecting an irritant solution (sclerotherapy) or by applying compression to reduce the pressure. Not all patients are suitable for, or agree to, venous surgery. Surgery on the deep veins is experimental, unevaluated and not widely practised.

Until recently the main aim of venous ulcer care has been to heal the ulcer. The use of high-compression bandaging has increased ulcer healing rates and the use of these bandages is widespread (Cullum 2000). Increased success in treating venous ulcers has meant that more patients are at risk of ulcer recurrence. Twelve-month recurrence rates range between 26% and 69% (Monk 1982; Moffatt 1995; Vowden 1997).

Description of the intervention

There are many ways of applying compression, e.g. bandages, compression stockings or combinations of bandages and/or stockings. The interpretation of comparisons between compression systems is complicated by the lack of internationally agreed standards.

In the UK, stockings are classified according to the amount of force required to stretch them and hence the level of compression they can apply to a limb (Table 1). Even in the UK it appears that different specifications apply to hosiery supplied through hospitals and via community pharmacists. In addition, different classification systems are used in other countries. An international collaboration is developing an agreed classification of compression devices for use in clinical studies (Rabe 2008).

OBJECTIVES

To assess the effects of compression (socks, stockings, tights, bandages) in preventing recurrence of venous leg ulcers; and specifically to answer the following questions:

1. does compression (bandages or hosiery) prevent the recurrence of venous ulceration after healing?
2. if compression prevents the recurrence of venous ulceration, what evidence is there to recommend particular levels of compression (high, medium or low), types of compression (single-layer or multi-layer stockings; bandages or stockings; below knee socks, stockings or tights) or brands of compression to prevent ulcer recurrence after healing?

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) which compare:

1. compression with no compression;
2. different strengths of compression;
3. different lengths of compression hosiery (below knee versus above knee/thigh length);
4. compression bandages with compression hosiery;
5. different types or brands of compression hosiery;
6. different types of compression regimens (e.g. long stretch, short stretch, single layer).

There was no restriction on publication status, date or language.

Types of participants

People with healed venous leg ulcers. We accepted trialists' inclusion criteria regarding diagnosis of ulcers as venous in origin.

Types of interventions

Compression bandages or hosiery (tights, stockings or socks). Studies of intermittent pneumatic compression devices are not included in this review as they are being considered in another Cochrane Review (Nelson 2011).

Types of outcome measures

Primary outcomes

- Incidence of re-ulceration (break in the skin) anywhere on the treated leg, irrespective of cause.

Secondary outcomes

- Duration of episodes of re-ulceration.
- Proportion of follow-up period for which the patient is ulcer-free.
- Incidence of ulceration on the other leg (also referred to as the contralateral leg).
- Patient compliance and comfort.
- Cost of treatment.
- Quality of life.

Search methods for identification of studies

For details of the search methods used in the first update of this review see [Appendix 1](#).

Electronic searches

For this second update we searched the following electronic databases to find reports of relevant RCTs:

- The Cochrane Wounds Group Specialised Register (searched 4 September 2014);
- The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2014, Issue 8);

The Cochrane Wounds Group Specialised Register comprises references identified from comprehensive electronic database searches, handsearches of relevant journals and abstract books of conference proceedings.

We used the following search strategy in the Cochrane Central Register of Controlled Trials (CENTRAL):

```
#1 MeSH descriptor: [Leg Ulcer] explode all trees 1203
#2 ((varicose next ulcer*) or (venous next ulcer*) or (leg next ulcer*)
or (stasis next ulcer*) or (crural next ulcer*) or "ulcus cruris" or
"ulcer* cruris"):ti,ab,kw 1556
#3 #1 or #2 2051
#4 MeSH descriptor: [Stockings, Compression] explode all trees 157
#5 compression:ti,ab,kw 3866
#6 stocking* or hosiery:ti,ab,kw 810
#7 bandag*:ti,ab,kw 2281
#8 wrap*:ti,ab,kw 159
#9 #4 or #5 or #6 or #7 or #8 5837
#10 #3 and #9 640
```

There were no restrictions with respect to language, date of publication or study setting.

Searching other resources

We contacted experts in wound care and companies that produce compression stockings/bandages to enquire about unpublished, ongoing and recently published trials for the original version of this review. We scrutinised citations within obtained reviews and papers to identify additional studies.

Data collection and analysis

Selection of studies

One review author assessed titles and abstracts of all studies identified by the search process with respect to their relevance and design, according to the selection criteria. We obtained full versions of articles if, from this initial assessment, they satisfied the selection criteria. Those rejected were checked by another review author.

We checked full papers to identify those that fit the inclusion criteria. This was repeated independently by another review author to verify.

Data extraction and management

We extracted and summarised details of the studies using a pre-specified data extraction sheet. We contacted study authors to

minimise missing data. We included studies that were published in duplicate only once. Data were extracted by one review author and checked for accuracy by a second.

Assessment of risk of bias in included studies

For this review update two review authors independently assessed each included study using the Cochrane Collaboration tool for assessing risk of bias ([Higgins 2011](#)). This tool addresses six specific domains, namely sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and other issues (e.g. extreme baseline imbalance) (see [Appendix 5](#) for details of criteria on which the judgement was based). We assessed blinding and completeness of outcome data for each outcome separately. We completed a 'Risk of bias' table for each eligible study. We discussed any disagreement amongst all review authors to achieve a consensus.

Measures of treatment effect

We entered data into Cochrane RevMan software ([RevMan 2011](#)) and used this to analyse the data. We presented results with 95% confidence intervals (CI). We reported estimates for dichotomous outcomes (e.g. number of ulcers reported) as risk ratio (RR). Continuous data would have been reported as mean difference (MD) with 95% CI. and standardised mean difference (SMD) if different measures used. Methods of synthesising the studies depended on their quality, design and heterogeneity. We explored both clinical and statistical heterogeneity. In the absence of clinical and statistical heterogeneity (as identified by an I^2 statistic less than 50%) we applied a fixed-effect model to pool data. In the presence of statistical heterogeneity (as estimated by a I^2 statistic between 59 and 75%) we applied a random-effects model for meta-analysis ([Higgins 2003](#)). Where synthesis was inappropriate we undertook a narrative overview, for example in the presence of significant statistical heterogeneity (I^2 of more than 75%), or of clinical heterogeneity.

RESULTS

Description of studies

We retrieved 12 studies in full and four met the inclusion criteria for this review ([Franks 1995](#); [Vandongen 2000](#); [Nelson 2006](#); [Milic 2010](#)). These trials are described in the [Characteristics of included studies](#) tables. Two trials compared the effectiveness of moderate (e.g. UK class 2) and high (e.g. UK class 3) compression hosiery ([Nelson 2006](#); [Milic 2010](#)); one is published as a conference abstract only ([Milic 2010](#)). One trial assessed the effect of compression stockings in reducing the area of lipodermatosclerosis in patients with previous venous ulceration and also reported recurrence rates with and without compression ([Vandongen 2000](#)). One trial compared the effectiveness of two different brands of moderate (UK class 2) compression stockings in community leg ulcer clinics ([Franks 1995](#)). Eight studies were excluded (see [Characteristics of excluded studies](#)).

[Nelson 2006](#) defined a recurrence as a break in the skin of the leg persisting for at least six weeks (outcome assessor was not blinded). [Vandongen 2000](#) defined re-ulceration as any break in the skin in the area between the ankle and the knee. [Milic 2010](#) and [Franks 1995](#) did not define re-ulceration. Three trials were planned after calculation of an appropriate sample size ([Franks 1995](#); [Vandongen](#)

2000; Nelson 2006) although Milic 2010 does not report this aspect of trial design in their abstract.

Risk of bias in included studies

Details of the risk of bias of each individual study are included in the 'Risk of bias' tables and summarised in Figure 1.

Figure 1. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)
Franks 1995	+	-	?	+	-	-	?
Milic 2010	?	?	+	?	?	-	-
Nelson 2006	+	?	+	+	+	-	-
Vandongen 2000	?	?	-	+	?	-	-

Allocation

Two trials used a computer-generated randomisation sequence (Franks 1995; Nelson 2006) whilst the remaining two trials gave no description of the method of randomisation. Allocation concealment (i.e. the person recruiting the patients into the trial was unaware of which group they would be recruited to) was attempted through using a closed envelope system in Vandongen 2000 however it is not clear whether the envelopes were shuffled, numbered or logged. Whilst the trial by Nelson 2006 used a remote method of allocation by telephone there was a possibility of selection bias as the person randomising patient was occasionally

informed of the allocation of subsequent patients by the remote randomisation office (personal communication, Nelson). Franks 1995 used an open computer-generated randomisation list and therefore allocation was not concealed and Milic 2010 gave limited information and was deemed to be at unclear risk of bias for this domain.

Blinding

Blinding of participants and caregivers would not have been possible in any of the trials therefore all are at risk of performance bias. Blinding of the outcome assessor was not stated or described

in any of the trial reports. Assessors were not blinded in the trial by [Nelson 2006](#) (personal communication, Nelson).

Incomplete outcome data

[Franks 1995](#) was at unclear risk of bias for this domain as it was unclear if the total number of participants enrolled in the trial were included in the analyses. [Vandongen 2000](#) was at high risk of attrition bias because participants were withdrawn if they did not wear their stockings and this is likely to have influenced their reulceration outcome; 12 people withdrew from the stocking arm in the first 6 months for "stocking-related" reasons compared with 3 from the non-stocking arm (these 3 wanted to wear stockings). More patients then dropped out between 6 and 12 months and we have not analysed these data.

[Milic 2010](#) and [Nelson 2006](#) were at low risk of attrition bias having small number of withdrawals or having reported final outcome data on all participants.

Selective reporting

Expected outcomes were reported in all trials (low risk of bias) with the exception of [Milic 2010](#) who reported limited details of study methodology as the report is in abstract form only.

Other potential sources of bias

In [Nelson 2006](#), the treatment groups were reported to be comparable at baseline for age, sex, ulcer location and ulcer and general medical history. Baseline group comparability was not reported by [Vandongen 2000](#) or [Milic 2010](#). In [Franks 1995](#), patients allocated the class 2 Medi sock had a median ulcer duration of 5.7 months compared to a median of 2.0 months in the Scholl group. This may reflect a greater severity of ulcer disease in the Medi group, and did not appear to be adjusted for in the analysis. Other baseline characteristics, such as a history of deep vein thrombosis and mobility, were comparable.

Effects of interventions

Four trials met the review criteria. There was no disagreement between review authors in selection of included/excluded studies.

HOW THE RESULTS ARE PRESENTED AND WHAT THE TERMS MEAN

Results of dichotomous variables are presented as risk ratio (RR) with 95% confidence intervals (CI).

Risk ratio of recurrence is the ulcer recurrence rate in the experimental group divided by the ulcer recurrence rate in the control group and indicates the likelihood of an ulcer recurring with the experimental compression compared with a control treatment (no compression or an alternative). By definition the risk of an ulcer recurring in the control group is 1, so the risk ratio reduction associated with using the experimental stocking is $1-RR$. The risk ratio indicates the relative benefit of a therapy but not the actual benefit, i.e. it does not take into account the number of people who would have had an ulcer recurrence anyway. The absolute risk reduction (ARR) can be calculated by subtracting the recurrence rate in the experimental group from the recurrence rate in the control group. The ARR tells us how much the decrease in recurrence is due to the stocking, and its inverse is the number needed to treat, or NNT. Thus a recurrence rate of 50% with a control treatment, which decreased to 30% with an experimental stocking,

translates into an ARR of $50\% - 30\% = 20\%$ ($0.5 - 0.3 = 0.2$). The NNT is the inverse of 20% (or 0.2) and this is 5. In other words five patients would need to receive the experimental stocking to prevent one additional leg ulcer from developing.

The results are presented with reference to the original questions posed by the review:

1. Does the application of compression bandages or hosiery prevent recurrence after venous ulcers heal?

We identified one study that compared ulcer recurrence in people with and without compression. The trial was set up to assess the effect of compression stockings in reducing the area of lipodermatosclerosis in patients with previous venous ulceration and also reported recurrence rates with and without compression ([Vandongen 2000](#)). It found that compression with high compression hosiery (class 3: Venosan 2003) significantly reduced ulcer recurrence compared with no compression at six months follow up (RR 0.46, 95% CI 0.27 to 0.76, $p=0.003$, [Analysis 1.1](#)). These trialists also reported reulceration at 12 months however we have not reported or analysed this due to the high attrition bias (only 22 participants out of 72 randomised to the stocking arm were analysed at 12 months compared with 24 out of 81 randomised to the non-stocking arm; patients were withdrawn from the stocking arm if they did not wear their stockings (16/72) and their outcomes are not reported).

In a trial comparing two brands of UK class 2 compression hosiery, [Franks 1995](#) also report recurrence in compliant and non compliant people. It is not clear if this comparison was pre-specified and the likely presence of selection bias means that their comparison of wearing or not wearing compression hosiery is an observational study rather than a trial of compression per se. [Franks 1995](#) found a higher recurrence rate in partially and non-compliant patients (10/25 with partial compliance versus 1/4 with non-compliance versus 43/136 with full compliance). The study also reported greater recurrence in participants who were excluded from the trial as they were unable to wear compression stockings compared with all those who wore compression (11/17 in those excluded versus 58/171 with compression; RR 2.58, 95% CI 1.33 to 5.01) ([Franks 1995](#)). This trial provides some indirect evidence that compression reduces recurrence.

2. If compression prevents recurrence, what is the optimal level of compression?

One trial ([Nelson 2006](#)) with 300 patients, followed up every four months for five years, compared ulcer recurrence rates in patients allocated to moderate (UK Class 2) or high (UK class 3) compression hosiery. There was no statistically significant difference in recurrence rates (39% with Class 2 versus 32% with Class 3; RR 0.82, 95% CI 0.61 to 1.12, $p=0.22$) at five years ([Analysis 2.1](#)). A second study with three-year follow up ([Milic 2010](#)) found significantly reduced ulcer recurrence with high (UK Class 3) compared with moderate (UK Class 2) compression hosiery (RR 0.57, 95% CI 0.39 to 0.81, $p=0.002$) ([Analysis 2.2](#)). It was not appropriate to pool these two studies ($I^2 = 92\%$) and there is insufficient information reported in [Milic 2007](#) to allow potential explanations for the heterogeneity.

[Nelson 2006](#) and [Milic 2010](#) also reported patient compliance with stockings; in [Nelson 2006](#) the compliance was patient reported however the in [Milic 2010](#) it is unclear how compliance data

were collected). [Milic 2010](#) reported no significant difference in compliance between Class 2 and Class 3 (high-compression) hosiery. [Nelson 2006](#) reported significantly greater compliance with UK Class 2 hosiery than with UK Class 3 hosiery (RR of non-compliance with Class 2 compared with Class 3; 0.81, 95% CI 0.68 to 0.96) [Analysis 2.3](#).

3. To what extent does the type or brand of compression hosiery influence recurrence rates after healing?

[Franks 1995](#) compared two brands of UK Class 2 compression hosiery (Medi and Scholl) and found no statistically significant difference between the two groups for ulcer recurrence (RR 0.74, 95%CI 0.45 to 1.20) ([Analysis 3.1](#)).

DISCUSSION

Non-systematic reviews of the literature invariably state that compression hosiery reduces the recurrence of venous leg ulcers ([Capeheart 1996](#)). A small study in this review found that compression can reduce recurrence of venous ulcers for up to 12 months ([Vandongen 2000](#)) but in this trial ulcer recurrence was not the primary outcome (reduction in area of lipodermatosclerosis was) and there were also high rates of attrition and probable attrition bias. The use of compression after venous ulcer healing is now widespread and further trials with a non-compression comparison group are unlikely. There is evidence that people who fail to comply with compression hosiery have higher recurrence rates than those who do comply but this finding is less robust evidence of the effectiveness of compression than direct comparisons within randomised controlled trials would be.

The trials reporting the relative benefits of medium or high compression hosiery reported only event rates at trial completion, and not time to recurrence. Without such analysis it is not clear whether the contradictory results for these two trials are a consequence of the difference in the length of follow up. As recurrence of an ulcer is likely after healing, and this risk does not reduce, then a very long follow-up period would potentially miss clinically important differences in effectiveness. This would occur if a high compression sock delayed recurrence for significantly longer than a moderate compression sock, but by 5 years the differences in effects size was reduced. Therefore future studies need to report not only the risk of recurrence at study follow-up points, but also the time to recurrence, as this is likely to be important to patients and clinicians.

The trials by Nelson, Franks and Vandongen were conducted in different settings: hospital ([Nelson 2006](#)) and community ([Franks 1995](#); [Vandongen 2000](#)). The setting of [Milic 2010](#) is unclear. The Nelson study defined a recurrence as a break in the skin lasting for six weeks. Franks and Milic do not describe their definition of recurrence and Vandongen defines recurrence as any break in the skin between the ankle and the knee. These differences may account for some of the variation between studies. Two trials were conducted in the United Kingdom (UK) and used stockings which are approved for use by the UK Drug Tariff. It is unclear whether these results can be extrapolated to other countries where standards for stockings are different.

Given the prevalence of venous disease and the relatively large number of trials of compression for the treatment of ulceration

([Cullum 2000](#)) it is disappointing that so few trials appear to have been undertaken for the use of compression to prevent ulcer recurrence. Additional trials may have been carried out but are unpublished and their impact on these results is unknown. Prospective registration of trials would reduce any potential publication bias.

AUTHORS' CONCLUSIONS

Implications for practice

High compression hosiery appears to be more effective in reducing recurrence from venous leg ulceration than no compression. There is some evidence that high-compression hosiery is more effective than moderate-compression in prevention of ulcer recurrence in the medium term although less clear in the long term. Compliance is lower in people wearing high-compression stockings and a possible strategy would be to prescribe the highest level of compression that people will tolerate (at least UK Class 2).

Implications for research

More research is needed regarding acceptable modes of long-term compression therapy for people at risk of recurrent venous ulceration. Future trials need to consider interventions to help people wear compression since there is evidence that compression is effective in reducing re-ulceration but that a high proportion of patients are disinclined to wear it. In-depth qualitative research is needed to understand the patients perspective and explain low rates of concordance.

Future trials of maintenance compression therapy and interventions to promote concordance:

- should be large enough to detect clinically important differences in recurrence.
- should define ulcer recurrence clearly as there may be small skin breaks due to varicose eczema that can be confused with a true ulcer recurrence.
- report co interventions thoroughly including surgery, exercise advice and drug therapies.
- should use blinded outcome assessment.
- should employ survival analysis methods to assess time to recurrence.
- should incorporate economic evaluations.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES
Characteristics of included studies [ordered by study ID]

Franks 1995

Methods	RCT
Participants	166 patients with newly healed venous leg ulcers and who could apply a compression sock. People with "mild" arterial disease were eligible for inclusion.

Compression for preventing recurrence of venous ulcers (Review)

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Franks 1995 (Continued)

Patients allocated to Medi hosiery had longer pre-healing ulcer duration (5.7 months versus 2.0 months) than people in Scholl.
The trial was conducted within a community leg ulcer service

Interventions	1. Below knee (Medi) UK class 2 2. Below knee (Scholl) UK class 2
Outcomes	Ulcer recurrence; compliance (patient reported); adverse reactions. Ulcer recurrence (people) at 18 months: 1. 21%, 2. 34% (no significant difference) The actual number of recurrences for each group is not provided All types of skin irritation: 1. 23/92 (25%), 2. 26/74 (35%) (no significant difference) Could not apply hosiery: 1. 12/92 (13%), 2. 13/74 (18%) Could not remove hosiery: 1. 11/92 (12%), 2. 11/74 (15%)
Notes	An <i>a priori</i> sample size calculation was based on estimates of rate of reactions to stockings (20% versus 40%)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Comment: computer-generated (personal communication, Franks).
Allocation concealment (selection bias)	High risk	Comment: open randomisation list used (personal communication, Franks).
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: Data were reported as percentages. It is unclear if the total number enrolled was included in the analyses.
Selective reporting (reporting bias)	Low risk	Comment: Expected outcomes were reported
Other bias	High risk	Comment: Baseline imbalance: the median duration of ulcer before the study was almost 3 times longer in the Medi group. It is unclear why there were 20% fewer patients in the Scholl group.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Not possible to blind patients and personnel to the intervention.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: It was unclear who conducted the outcome assessment or if they were blinded to the allocation group

Milic 2010

Methods	RCT
Participants	338 patients with recently healed venous ulcers and no significant arterial disease, rheumatoid disease or diabetes mellitus (data analysed on 327 people who did comply with randomisation)
Interventions	1. Class 2 compression hosiery

Compression for preventing recurrence of venous ulcers (Review)

Milic 2010 (Continued)

2. Heelless, open toed Class 3 compression hosiery

Patients were instructed to wear compression stockings during the first year of the follow up during day and night. In the second and the third year of follow up, patients were instructed to wear elastic stockings only during the day.

Outcomes	Ulcer recurrence; compliance with treatment. Ulcer recurrence at 3 years: 1. 59/162 (36.4%) with class 2 versus 34/165 (20.6%) with class 3
Notes	3-year follow up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomized into two groups were 338 patients" Comment: No information about sequence generation; abstract only.
Allocation concealment (selection bias)	Unclear risk	Quote: "Randomized into two groups were 338 patients" Comment: No information about allocation concealment; abstract only.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Eleven patients did not comply with their randomized compression class, eight (4.6%) in class 3 and three (1.8%) in class 2." Comment: whilst not explicitly stated, 11 participants were excluded from the analysis - presumably these 11 however this is only 3.3% of those randomised.
Selective reporting (reporting bias)	Unclear risk	Comment: Abstract only. Limited details of study methodology although expected outcomes are reported.
Other bias	Unclear risk	Comment: Abstract only Limited details of study methodology.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Blinding of intervention not possible.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "An open, prospective, randomized, single-center study..." Comment: Unblinded study; described as 'open'.

Nelson 2006

Methods	RCT
Participants	300 people with recently healed venous leg ulcers. Trial setting was a hospital leg ulcer clinic.
Interventions	1. UK class 2 compression hosiery (moderate compression) 2. UK class 3 compression hosiery (high compression) Each patient was measured for hosiery by an orthotist. Patients had a check up and resupply of hosiery every 4 months. Telephone hot-line to leg ulcer clinic in case of problems.
Outcomes	Primary outcome: time to ulceration; ulceration, defined as a skin break in the same leg, that failed to heal after 6 weeks' treatment.

Nelson 2006 (Continued)

Compliance: compliant patients were defined as those who wore the allocated class of hosiery throughout the study, otherwise classed as "non-compliant".

Incidence of major recurrence (defined as a skin break for a minimum of 6 weeks) at 60 months

1. 59/151 (39%)

2. 48/149 (32%)

No significant difference (Cox proportional hazards model)

Notes An *a priori* sample size calculation was reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote (from personal communication): "Computer-generated" (personal communication, Nelson)
Allocation concealment (selection bias)	Unclear risk	Quote: "We used telephone allocation ... During the trial follow-up, however, we were informed that on at least one occasion the allocation concealment was not maintained by the telephone service because both the leg ulcer clinic and the telephone service were extremely busy; therefore the allocations for two patients were supplied "in order to save time". Comment: It is unclear how often this occurred.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Our analyses were conducted on an intention to treat basis".
Selective reporting (reporting bias)	Low risk	Comment: Expected outcomes were reported
Other bias	Low risk	
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Blinding of staff and patients to the intervention is not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: The outcome assessor was not blinded to the allocation group (personal communication Nelson)

Vandongen 2000

Methods	RCT
Participants	153 patients with recently healed venous leg ulcer (2 weeks previously)
Interventions	1. Compression stockings (Venosan 2003) 2. No compression stockings
Outcomes	Incidence of ulcer recurrence at 6 months and 12 months however the 12 month data are incomplete and subject to heavy attrition bias (there was a total of 16 stocking related withdrawals from the stocking group i.e., refusal to wear stockings; their outcomes are not known but re-ulceration rates likely to be high - cannot assume they did not reulcerate).

Vandongen 2000 (Continued)

1. 6 months: 15/72 (21%) with compression versus 37/81 (46%) with no compression

Notes	12 month follow up data not analysed due to attrition bias.	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomisation was by a closed envelope system". Comment: No description of method of sequence generation; if envelopes were shuffled, sequentially numbered etc.
Allocation concealment (selection bias)	Unclear risk	Quote: "Randomisation was by a closed envelope system. The envelopes were only opened after all inclusion criteria had been met". Comment: The security of this method is not clear from the reporting. Low risk if envelopes were sequentially numbered and a log kept; high risk if not.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "Patients were withdrawn from the study if they were non-compliant with the treatment..." (Materials and Methods) Quote: "A total of 16 patients in the stocking group refused to continue wearing stockings whereas 3 patients in the no stocking group withdrew so that they could wear stockings". (Results). Comment: Re-ulceration outcomes are not known for withdrawn patients. A much greater proportion of patients withdrew from the stocking arm and their re-ulceration rates are likely to be high but are not known.
Selective reporting (reporting bias)	Low risk	Comment: Expected outcomes are reported
Other bias	Unclear risk	Comment: Participants in this trial were participating in a randomised trial of longer follow-up, assessing the role of elastic compression stockings in preventing recurrent venous ulceration; only those with healed ulcers who consented were randomised for this study.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Personnel and participants could not be blinded to treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: Process of outcome assessment (for re-ulceration) not described. Blinding of outcome assessors not mentioned but unlikely.

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Gohel 2005	Compares compression versus compression + surgery. Includes both healed and open ulcers, therefore it is a study of surgery not compression

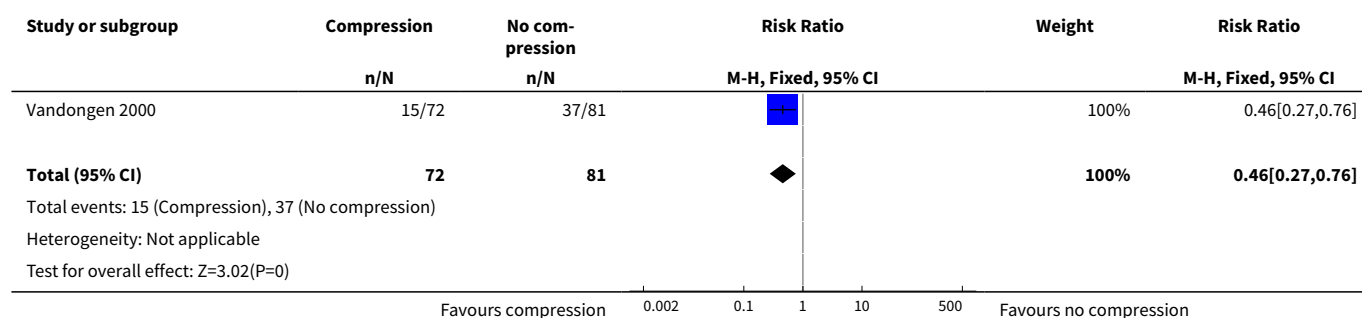
Study	Reason for exclusion
Iglesias 2004	Has recurrence data but there was no systematic allocation to one type or other of compression hosiery and therefore does not answer this question. This is an observational study with regards to recurrence
Junger 2002	No recurrence data
Junger 2006	Clinical outcomes not measured and no recurrence data
Lewis 1976	Outcome was not ulcer recurrence
Milic 2007	Study was not randomised
Moffatt 2003	No recurrence data
Polignano 2004	No recurrence data

DATA AND ANALYSES

Comparison 1. Compression hosiery versus no compression

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of recurrence at 6 months	1	153	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.27, 0.76]


Analysis 1.1. Comparison 1 Compression hosiery versus no compression, Outcome 1 Incidence of recurrence at 6 months.





Comparison 2. Class 3 compression hosiery versus class 2 compression hosiery

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of recurrence at 5 years follow up	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2 Incidence of recurrence at 3 years follow up	1	327	Risk Ratio (M-H, Fixed, 95% CI)	0.57 [0.39, 0.81]
3 Compliance	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected



Analysis 2.1. Comparison 2 Class 3 compression hosiery versus class 2 compression hosiery, Outcome 1 Incidence of recurrence at 5 years follow up.

Study or subgroup	Class 3 n/N	Class 2 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Nelson 2006	48/149	59/151		0%	0.82[0.61,1.12]
			Favours Class 3 0.02 0.1 1 10 50 Favours Class 2		

Analysis 2.2. Comparison 2 Class 3 compression hosiery versus class 2 compression hosiery, Outcome 2 Incidence of recurrence at 3 years follow up.

Study or subgroup	Class 3 n/N	Class 2 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Milic 2010	34/165	59/162		100%	0.57[0.39,0.81]
Total (95% CI)	165	162		100%	0.57[0.39,0.81]
Total events: 34 (Class 3), 59 (Class 2)					
Heterogeneity: Not applicable					
Test for overall effect: Z=3.08(P=0)					
			Favours Class 3 0.005 0.1 1 10 200 Favours Class 2		

Analysis 2.3. Comparison 2 Class 3 compression hosiery versus class 2 compression hosiery, Outcome 3 Compliance.

Study or subgroup	Class 3	Class 2	Risk Ratio	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI	M-H, Random, 95% CI
Milic 2010	157/165	159/162		0.97[0.93,1.01]
Nelson 2006	86/149	108/151		0.81[0.68,0.96]
			Favours Class 3 0.5 0.7 1 1.5 2 Favours Class 2	

Comparison 3. Comparison between different brands of compression hosiery (class 2)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of recurrence at 18 months	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Analysis 3.1. Comparison 3 Comparison between different brands of compression hosiery (class 2), Outcome 1 Incidence of recurrence at 18 months.

Study or subgroup	Medi n/N	Scholl n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Franks 1995	22/92	24/74		0%	0.74[0.45,1.2]
Favours Medi brand			0.005 0.1 1 10 200	Favours Scholl brand	

ADDITIONAL TABLES

Table 1. Classification of compression stockings (UK)

Class	Descriptor	Ankle pressure	Indication
Class 1	Light support	14 to 17 mmHg	Used to treat varicose veins
Class 2	Medium support	18 to 24 mmHg	Used to treat severe chronic hypertension and severe varicose veins, and to prevent venous leg ulcers
Class 3	Strong support	25 to 35 mmHg	Used to treat more severe varicosities and to prevent venous leg ulcers

APPENDICES

Appendix 1. Search methods for first update 2012

For the first update we searched the following electronic databases to find reports of relevant RCTs:

- The Cochrane Wounds Group Specialised Register (searched 1 March 2012);
- The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2012, Issue 2);
- Ovid MEDLINE (1950 to February Week 4 2012);
- Ovid MEDLINE (In-Process & Other Non-Indexed Citations, February 29, 2012);
- Ovid EMBASE (1980 to 2012 Week 08);
- EBSCO CINAHL (1982 to 1 March 2012).

We used following search strategy in the Cochrane Central Register of Controlled Trials (CENTRAL):

```
#1 MeSH descriptor Varicose Ulcer explode all trees
#2 MeSH descriptor Leg Ulcer explode all trees
#3 (varicose NEXT ulcer*) or (venous NEXT ulcer*) or (leg NEXT ulcer*) or (stasis NEXT ulcer*) or ((lower NEXT extremity*) NEAR/2 ulcer*) or (crural NEXT ulcer*) or "ulcus cruris":ti,ab,kw
#4 (#1 OR #2 OR #3)
#5 MeSH descriptor Stockings, Compression explode all trees
#6 MeSH descriptor Occlusive Dressings explode all trees
```

```
#7 compression:ti,ab,kw
#8 stocking* or hosiery:ti,ab,kw
#9 bandag*:ti,ab,kw
#10 wrapp*:ti,ab,kw
#11 (#5 OR #6 OR #7 OR #8 OR #9 OR #10)
#12 (#4 AND #11)
```

The search strategies for Ovid MEDLINE, Ovid EMBASE and EBSCO CINAHL can be found in [Appendix 2](#); [Appendix 3](#) and [Appendix 4](#) respectively. We combined the Ovid MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximising version (2008 revision) ([Lefebvre 2011](#)). We combined the Ovid EMBASE and EBSCO CINAHL searches with the trial filters developed by the Scottish Intercollegiate Guidelines Network (SIGN) ([SIGN 2011](#)). Overall there were no restrictions with respect to language, date of publication or study setting.

Appendix 2. Ovid MEDLINE search strategy

```
1 exp Varicose Ulcer/ (1742)
2 exp Leg Ulcer/ (9252)
3 (varicose ulcer* or venous ulcer* or leg ulcer* or stasis ulcer* or (lower extremit* adj ulcer*) or crural ulcer* or ulcus cruris).tw. (3522)
4 or/1-3 (9929)
5 exp Stockings, Compression/ (708)
6 exp Occlusive Dressings/ (1506)
7 compression.tw. (36016)
8 stocking*.tw. (1844)
9 hosiery.tw. (115)
10 bandag*.tw. (1965)
11 wrapp*.tw. (3800)
12 or/5-11 (43752)
13 4 and 12 (1046)
14 randomized controlled trial.pt. (223436)
15 controlled clinical trial.pt. (38045)
16 randomized.ab. (180248)
17 placebo.ab. (85725)
18 clinical trials as topic.sh. (75431)
19 randomly.ab. (124303)
20 trial.ti. (66225)
21 or/14-20 (506202)
22 Animals/ (2317036)
23 Humans/ (6394714)
24 22 not 23 (1517998)
25 21 not 24 (461747)
26 13 and 25 (220)
```

Appendix 3. Ovid EMBASE search strategy

```
1 exp Varicosis/ (18194)
2 exp Leg Ulcer/ (5503)
3 (varicose ulcer* or venous ulcer* or leg ulcer* or stasis ulcer* or (lower extremit* adj ulcer*) or crural ulcer* or ulcus cruris).tw. (5041)
4 or/1-3 (24417)
5 exp Compression Therapy/ (5030)
6 compression.tw. (49673)
7 (stocking* or hosiery).tw. (2890)
8 bandag*.tw. (2777)
9 wrapp*.tw. (4882)
10 or/5-9 (60189)
11 4 and 10 (2119)
12 exp Clinical trial/ (717496)
13 Randomized controlled trial/ (249723)
14 Randomization/ (46062)
15 Single blind procedure/ (13423)
16 Double blind procedure/ (76668)
17 Crossover procedure/ (27602)
18 Placebo/ (145528)
19 Randomi?ed controlled trial$.tw. (65694)
```

20 RCT.tw. (8198)
 21 Random allocation.tw. (797)
 22 Randomly allocated.tw. (12238)
 23 Allocated randomly.tw. (1087)
 24 (allocated adj2 random).tw. (244)
 25 Single blind\$.tw. (8219)
 26 Double blind\$.tw. (78286)
 27 ((treble or triple) adj blind\$).tw. (193)
 28 Placebo\$.tw. (118364)
 29 Prospective study/ (158978)
 30 or/12-29 (951700)
 31 Case study/ (12185)
 32 Case report.tw. (143481)
 33 Abstract report/ or letter/ (464948)
 34 or/31-33 (617042)
 35 30 not 34 (925550)
 36 animal/ (575778)
 37 human/ (7453977)
 38 36 not 37 (392008)
 39 35 not 38 (906272)
 40 11 and 39 (560)

Appendix 4. EBSCO CINAHL search strategy

S12 S4 and S11
 S11 S5 or S6 or S7 or S8 or S9 or S10
 S10 TI wrapp* or AB wrapp*
 S9 TI bandag* or AB bandag*
 S8 TI (stocking* or hosiery) or AB (stocking* or hosiery)
 S7 TI compression or AB compression
 S6 (MH "Bandaging Techniques+")
 S5 (MH "Compression Therapy")
 S4 S1 or S2 or S3
 S3 lower extremity N3 ulcer* or AB lower extremity N3 ulcer*
 S2 TI (varicose ulcer* or venous ulcer* or leg ulcer* or stasis ulcer* or crural ulcer*) or AB (varicose ulcer* or venous ulcer* or leg ulcer* or stasis ulcer* or crural ulcer*)
 S1 (MH "Leg Ulcer+")

Appendix 5. Risk of bias criteria

1. Was the allocation sequence randomly generated?

Low risk of bias

The investigators describe a random component in the sequence generation process such as: referring to a random number table; using a computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots.

High risk of bias

The investigators describe a non-random component in the sequence generation process. Usually, the description would involve some systematic, non-random approach, for example: sequence generated by odd or even date of birth; sequence generated by some rule based on date (or day) of admission; sequence generated by some rule based on hospital or clinic record number.

Unclear

Insufficient information about the sequence generation process to permit judgement of low or high risk of bias.

2. Was the treatment allocation adequately concealed?

Low risk of bias

Participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based and pharmacy-controlled randomisation); sequentially-numbered drug containers of identical appearance; sequentially-numbered, opaque, sealed envelopes.

High risk of bias

Participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or nonopaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure.

Unclear

Insufficient information to permit judgement of low or high risk of bias. This is usually the case if the method of concealment is not described or not described in sufficient detail to allow a definite judgement, for example if the use of assignment envelopes is described, but it remains unclear whether envelopes were sequentially numbered, opaque and sealed.

3. Blinding - was knowledge of the allocated interventions adequately prevented during the study?**Low risk of bias**

Any one of the following.

- No blinding, but the review authors judge that the outcome and the outcome measurement are not likely to be influenced by lack of blinding.
- Blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken.
- Either participants or some key study personnel were not blinded, but outcome assessment was blinded and the non-blinding of others unlikely to introduce bias.

High risk of bias

Any one of the following.

- No blinding or incomplete blinding, and the outcome or outcome measurement is likely to be influenced by lack of blinding.
- Blinding of key study participants and personnel attempted, but likely that the blinding could have been broken.
- Either participants or some key study personnel were not blinded, and the non-blinding of others likely to introduce bias.

Unclear

Any one of the following.

- Insufficient information to permit judgement of low or high risk of bias.
- The study did not address this outcome.

4. Were incomplete outcome data adequately addressed?**Low risk of bias**

Any one of the following.

- No missing outcome data.
- Reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias).
- Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate.
- For continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size.
- Missing data have been imputed using appropriate methods.

High risk of bias

Any one of the following.

- Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups.
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate.
- For continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size.
- 'As-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation.

- Potentially inappropriate application of simple imputation.

Unclear

Any one of the following.

- Insufficient reporting of attrition/exclusions to permit judgement of low or high risk of bias (e.g. number randomised not stated, no reasons for missing data provided).
- The study did not address this outcome.

5. Are reports of the study free of suggestion of selective outcome reporting?**Low risk of bias**

Any of the following.

- The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way.
- The study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon)

High risk of bias

Any one of the following.

- Not all of the study's pre-specified primary outcomes have been reported.
- One or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not pre-specified.
- One or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect).
- One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis.
- The study report fails to include results for a key outcome that would be expected to have been reported for such a study.

Unclear

Insufficient information to permit judgement of low or high risk of bias. It is likely that the majority of studies will fall into this category.

6. Other sources of potential bias:**Low risk of bias**

The study appears to be free of other sources of bias.

High risk of bias

There is at least one important risk of bias. For example, the study:

- had a potential source of bias related to the specific study design used; or
- had extreme baseline imbalance; or
- has been claimed to have been fraudulent; or
- had some other problem.

Unclear

There may be a risk of bias, but there is either:

- insufficient information to assess whether an important risk of bias exists; or
- insufficient rationale or evidence that an identified problem will introduce bias.

WHAT'S NEW

Date	Event	Description
5 September 2014	New search has been performed	Second update, new search no new trials identified.
5 September 2014	New citation required but conclusions have not changed	Conclusions remain unchanged.

HISTORY

Protocol first published: Issue 3, 2000

Review first published: Issue 4, 2000

Date	Event	Description
28 June 2012	New search has been performed	New searches, two trials added (Vandongen 2000 ; Milic 2010).
28 June 2012	New citation required and conclusions have changed	'Risk of bias' tables completed. Conclusions strengthened.
18 June 2008	Amended	Converted to new review format.
23 August 2000	New citation required and conclusions have changed	Substantive amendment.

CONTRIBUTIONS OF AUTHORS

EAN drafted the protocol; checked the literature search results against inclusion criteria; made initial decisions about inclusion; extracted data; undertook quality assessment and initial analysis; drafted the review and updated the review.

SBS checked inclusion decisions; checked data extraction and quality assessment, approved the review and undertook the second update of the review.

Contributions of editorial base:

Nicky Cullum: edited the review, advised on methodology, interpretation and review content. Approved and edited the final review version prior to submission and the first update.

Amanda Briant: ran the searches and checked the search methods section for the update.

DECLARATIONS OF INTEREST

E Andrea Nelson was a trialist ([Nelson 2006](#)). Sally Bell-Syer - none.

SOURCES OF SUPPORT

Internal sources

- Department of Health Sciences, University of York, UK.
- School of Healthcare, University of Leeds, UK.

External sources

- NHS Health Technology Assessment Programme, England, UK.
- NIHR/Department of Health (England), (Cochrane Wounds Group), UK.

INDEX TERMS

Medical Subject Headings (MeSH)

*Stockings, Compression; Compression Bandages; Randomized Controlled Trials as Topic; Risk; Secondary Prevention; Time Factors; Varicose Ulcer [*prevention & control]

MeSH check words

Adult; Humans